UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/111,123	07/06/1998	HABIB ZAGHOUANI	8114-005-WO-CIP	5474

32301 7590 08/24/2006

CATALYST LAW GROUP, APC
9710 SCRANTON ROAD, SUITE S-170
SAN DIEGO, CA 92121

EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/111,123	ZAGHOUANI, HABIB	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 21-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7 and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received April 27, 2006 are acknowledged.

Claims 1 and 21have been amended.

Claims 8-20 have been canceled.

Claims 1, 3-7, and 21-27 are pending and under examination as they read on fusion proteins comprising immunoglobulins and T cell receptor antagonists.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. The rejection of claims 1, 3-4, and 21-24 under 35 U.S.C. 102(e) as being anticipated by Deo et al., (U.S. Patent Number 5,837,243, of record,) as evidenced by Ukkonen et al. (J. Exp. Med, 1986, 163:952-971, see entire document) and as evidenced by Kuby (Immunology, 1992, W.H. Freeman and company, pages 208-211,

see entire selection) has been withdrawn due to applicant's claim amendments received April 27, 2006.

Applicant argues that Deo et al. do not teach an immunoglobulin fusion protein wherein a T cell antagonist has been used to replace a complementarity-determining region of immunoglobulin. In view of the claim amendments received April 27, 2006, and upon consideration of the teachings of Deo et al. this argument is convincing and therefore rejection of record is withdrawn.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The rejection of claims 1, 5, 21 and 25 under 35 U.S.C. 103(a) as being unpatentable over Deo et al., (U.S. Patent Number 5,837,243, of record, see entire document) in view of Karin et al. (J. Exp. Med, 1994, 180: 2227-2237,of record, see entire document) has been withdrawn due to applicant's claim amendments received April 27, 2006.

Specifically, the primary reference Deo et al. does not teach an immunoglobulin fusion protein wherein a T cell antagonist has been used to replace a complementarity-determining region of immunoglobulin.

7. The rejection of claims 1, 6, 21 and 26 under 35 U.S.C. 103(a) as being unpatentable over Deo et al., (U.S. Patent Number 5,837,243,of record, see entire document) in view of Kuchroo et al., (J. Immunol. 1994, 153: 3326-3336, of record, see entire document) has been withdrawn due to applicant's claim amendments received April 27, 2006.

Specifically, the primary reference Deo et al. does not teach an immunoglobulin fusion protein wherein a T cell antagonist has been used to replace a complementarity-determining region of immunoglobulin.

8. The rejection of claims 1, 7, 21 and 27 under 35 U.S.C. 103(a) as being unpatentable over Deo et al., U.S. Patent Number 5,837,243 in view of Elliott et al. (J. Clin. Invest., 1996, 98: 1602-1612), Kuchroo et al., (J. Immunol. 1994, 153: 3326-3336) and Karin et al. (J. Exp. Med, 1994, 180: 2227-2237) has been withdrawn due to applicant's claim amendments received April 27, 2006.

Specifically, the primary reference Deo et al. does not teach an immunoglobulin fusion protein wherein a T cell antagonist has been used to replace a complementarity-determining region of immunoglobulin.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1, 3-4, 6, 21-24 and 26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,737,057. Although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons previously of record.

The office action mailed August 10, 2004 states that:

> The claims of U.S. Patent No. 6,737,057 teach a composition comprising an immunoglobulin linked to a peptide that can bind an Fc receptor, be endocytosed, processed and presented in the context of MHC Class II molecules for the purpose of preventing the activation of autoreactive T cells *in vivo*. The claims of U.S. Patent No. 6,737,057 also teach the use of a human immunoglobulin protein and the incorporation of a T cell antagonist from proteolipid protein. The claims of the instant application recite a fusion protein for the treatment of an autoimmune disorder comprising an immunoglobulin linked to a peptide that can bind an Fc receptor, be endocytosed, processed and presented in the context of MHC Class II molecules for the purpose of preventing the activation of autoreactive T cells. Patients have symptoms associated with an autoimmune disorder that require alleviation, thus necessitating that the fusion protein of the instant application be used *in vivo*. The fusion protein of the instant application cannot be administered to a patient for the treatment of an autoimmune disorder without first placing it into a solution or adding it into a pill, thus making it a composition. Therefore, the instantly pending claims are obvious in view of claims 1-16 of U.S. Patent No. 6,737,057.

Applicant's arguments filed April 27, 2006 have been fully considered but they are not persuasive. Applicant argues that the patented claims do not recite an immunoglobulin wherein a CDR of the immunoglobulin is replaced with a T cell epitope.

This argument is unpersuasive because of patented claim 7 which recites wherein "... a T cell receptor antagonist is positioned within at least one complementarity-determining region to partially or fully replace said complementarity determining region."

The rejection of record is maintained.

11. The following are new grounds of rejection necessitated by applicant's claim amendments received April 27, 2006.

Claim Rejections - 35 USC § 103

12. Claims 1, 3, 4, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al. (US Patent 5,837,243, of record) in view of Zanetti et al. (WO 90/09804).

Deo et al. teach fusion proteins comprising an immunoglobulin and a TCR antagonist that are to be used in the treatment of autoimmune diseases such as rheumatoid arthritis and multiple sclerosis (see entire document, particularly lines 7-27 of column 33). These fusion proteins are disclosed as being humanized and thus comprise at least a portion of human IgG (see particularly lines 1-13 of column 7). These teachings differ from the instant claimed invention in that Deo et al. do not replace a CDR of the immunoglobulin molecule with a TCR antagonist.

Zanetti et al. teach fusion proteins that are to be used for treating autoimmune diseases (see entire document, particularly the abstract). Their fusion proteins are immunoglobulins comprising epitopes that have been substituted for a complementarity determining region (CDR) of an immunoglobulin (see particularly lines 21-25 of page 22). Such fusion proteins are advantageous because they retain the functionality of the C-terminus constant domain of the immunoglobulin heavy chain which allows localization of the fusion protein to specific cellular receptors and because they retain the specific reactivity of the introduced novel antigenic determinant or epitope (see particularly lines 1-25 of page 5).

Therefore, in would have been prima facie obvious to a person of ordinary skill at the time the invention was made to make a fusion protein comprising an immunoglobulin wherein a CDR has been replaced with a TCR antagonist peptide. A person of ordinary skill in the art at the time the invention was made would have been motivated to make such a fusion protein since immunoglobulins comprising TCR antagonists are useful in treating autoimmune diseases as taught by Deo et al., and Zanetti et al. teach that fusion proteins comprising epitopes in the CDR are advantageous because they retain the functional activities of the immunoglobulin heavy chain constant domain and the activity of the heterologous epitope.

13. Claims 5 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Claims 1, 3, 4, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al. (US Patent 5,837,243, of record) in view of Zanetti et al. (WO 90/09804) as applied to claims 1, 3, 4, and 21-24 above, and further in view of Karin et al. (J. Exp.

Med, 1994, 180: 2227-2237, of record) and in view of Bona et al. (Cellular and Molecular Biology, 1994, 40:21-30, of record).

The teachings of Deo et al. in view of Zanetti et al. have been discussed above. These teachings differ from the claimed invention in that they do not specify the protein from which the TCR antagonist is derived for treating autoimmune diseases such as rheumatoid arthritis and multiple sclerosis.

Karin et al. teach that myelin basic protein (MBP) is a major target of autoreactive T cells in multiple sclerosis (MS) and its mouse model system experimental allergic encephalomyelitis (EAE), and teach the use of T cell receptor antagonist peptides derived from MBP for the treatment of MS and EAE (see entire document, particularly the abstract and the last sentence of the right column of page 2235).

Bona et al. teach that fusion proteins comprising an immunoglobulin wherein a CDR is replaced with a peptide epitope offer the advantage of longer half-life as compared to the peptide itself when used in therapeutic methods (see entire document, particularly the top of the right column of page 23).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make fusion proteins comprising an immunoglobulin wherein a CDR has been replaced with a TCR antagonists derived from MBP. Motivation to place the TCR antagonist peptide into an immunoglobulin fusion protein comes from the teachings of Karin et al. that their MBP derived antagonists are effective in treating MS and EAE and the teachings of Bona et al. that immunoglobulin fusion proteins are more advantageous than peptides in methods of treatment due to the longer half-life of such fusion proteins as compared to peptides, and as such the resulting fusion protein would have a longer in vivo half-life as compared to the free peptide. A person of ordinary skill in the art would have been further motivated to make an immunoglobulin fusion protein comprising the TCR antagonist peptide of Karin et al. wherein a CDR of the immunoglobulin is replaced with the antagonist peptide based on the teachings of Deo et al. and Zanetti et al. that fusion immunoglobulins comprising such a structure have the advantage of retaining the function properties of the immunoglobulin heavy chain and the introduced epitope and because Deo et al. and

Zanetti et al. teach that immunoglobulins comprising the replacement of a CDR with a TCR antagonist peptide are to be used in methods of treating the autoimmune disease multiple sclerosis.

14. Claims 6 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al. (US Patent 5,837,243, of record) in view of Zanetti et al. (WO 90/09804) as applied to claims 1, 3, 4, and 21-24 above, and further in view of Kuchroo et al. (J. Immunol., 1994, 153:3326-3336, of record) and in view of Bona et al. (Cellular and Molecular Biology, 1994, 40:21-30, of record).

The teachings of Deo et al. in view of Zanetti et al. have been discussed above. These teachings differ from the claimed invention in that they do not specify the protein from which the TCR antagonist is derived for treating autoimmune diseases such as rheumatoid arthritis and multiple sclerosis.

Kuchroo et al. teach that T cell receptor antagonist peptides derived from proteolipid protein (PLP) can be successfully used to treat EAE, a mouse model of MS (see entire document, particularly the abstract).

Bona et al. teach that fusion proteins comprising an immunoglobulin wherein a CDR is replaced with a peptide epitope offer the advantage of longer half-life as compared to the peptide itself when used in therapeutic methods (see entire document, particularly the top of the right column of page 23).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make fusion proteins comprising an immunoglobulin wherein a CDR has been replaced with a TCR antagonists derived from PLP. Motivation to place the TCR antagonist peptide into an immunoglobulin fusion protein comes from the teachings of Kuchroo et al. that their PLP derived antagonists are effective in treating EAE, a mouse model of MS, and the teachings of Bona et al. that immunoglobulin fusion proteins are more advantageous than peptides in methods of treatment due to the longer half-life of such fusion proteins as compared to peptides, and as such the resulting fusion protein would have a longer in vivo half-life as compared to the peptide. A person of ordinary skill in the art would have been further

motivated to make an immunoglobulin fusion protein comprising the TCR antagonist peptides of Kuchroo et al. wherein a CDR of the immunoglobulin is replaced with the antagonist peptide based on the teachings of Deo et al. and Zanetti et al. that fusion immunoglobulins comprising such a structure have the advantage of retaining the function properties of the immunoglobulin heavy chain and the introduced epitope and because Deo et al. and Zanetti et al. teach that immunoglobulins comprising the replacement of a CDR with a TCR antagonist peptide are to be used in methods of treating the autoimmune disease multiple sclerosis.

15. Claims 7 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deo et al. (US Patent 5,837,243, of record) in view of Zanetti et al. (WO 90/09804) in view of Karin et al. (J. Exp. Med, 1994, 180: 2227-2237, of record, see entire document), in view of Kuchroo et al. (J. Immunol., 1994, 153:3326-3336, of record) and in view of Bona et al. (Cellular and Molecular Biology, 1994, 40:21-30, of record) as applied to claims 1, 3-6, and 21-26 above, and further in view of Elliott et al. (J. Clin. Invest., 1996, 98: 1602-1612, of record).

The teachings of Deo et al., Zanetti et al., Karin et al., Kuchroo et al., and Bona et al. have been discussed above. These teachings differ from the instant claimed invention in that TCR antagonists from PLP and MBP are not simultaneously present in a fusion protein.

Elliott et al. teach that fusion construct comprising multiple epitopes are more effective than using a single epitope in treating autoimmune diseases, and fusion protein comprising epitopes from MBP and PLP that is effective in treating EAE, a mouse model of MS (see entire document, particularly the abstract and the first and second full paragraphs of the left column of page 1611).

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make a fusion protein comprising an immunoglobulin and a TCR antagonist as taught by Deo et al., Zanetti et al., Karin et al. Kuchroo et al. and Bona et al. that comprises antagonists derived from both MBP and PLP. A person of ordinary skill in the art would have been motivated at the time the

invention was made to include more than one peptide epitope into an immunoglobulin fusion protein because Elliott et al. teach that its is clinically more advantageous to simultaneously target multiple epitopes as compared to targeting a single epitope in methods of treating autoimmune diseases such as EAE and MS.

16. No claims are allowed.

17. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
August 16, 2006

8/19/06

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER